al., *Cancer Chemother. Pharmacol., 34,* S58 (1994); Kingston et al., U.S. Patent No. 5,278,324).

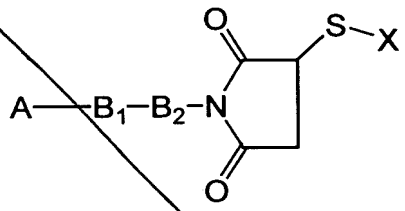
IN THE CLAIMS:

Please cancel claims 64, 67, 71, 74, 78, 82, 88 and 89 without prejudice to reinstate.

Please cancel claims 92-106 as directed towards a non-elected invention.

Please amend claims 63, 65, 68, 77, 79, 80, 81 and 83 to read as follows:

63. (Amended) A water-soluble compound of the formula



wherein:

A is a water-insoluble drug selected from the group consisting of a macrolide and an ansamacrolide;

B_1 and B_2 together are a spacer moiety,

wherein B_1 is selected from the group consisting of a methylenyl, an amido, -N=, an amino, and a thiol maleimido, and

B_2 is selected from the group consisting of a C_1-C_{19} alkylamido, a C_1-C_{19} alkyl, a C_2-C_{19} alkenyl, a C_2-C_{19} alkynyl, a C_1-C_{19} hydroxyalkyl, a C_1-C_{19} alkyl carbamoyl, a C_1-C_{19} alkylcarbonyl, and an aralkyl, any of which can be further substituted with one or more substitutents, which can be the same or different, selected from the group consisting of a nitro, a halo, an azido, a hydroxy, an amido, and an amino group; and

X is a polar moiety selected from the group consisting of an amino acid, a peptide, a polypeptide, and a protein;

or a pharmaceutically acceptable salt of said compound.

65. (Amended) The compound of claim 63, wherein

B_2 is selected from the group consisting of a C_1-C_7 alkylamido, a C_1-C_7 alkyl, a C_2-C_7 alkenyl, a C_2-C_7 alkynyl, a C_1-C_7 hydroxyalkyl, a C_1-C_7 alkyl carbamoyl, a C_1-C_7 alkylcarbonyl, and an aralkyl, any of which can be further substituted with one or more substituents, which can be the same or different, selected from the group consisting of a nitro, a halo, an azido, a hydroxy, an amido and an amino group.

68. (Amended) The compound of claim 63, wherein said polar moiety is L-cysteine.

77. (Amended) A method of treating cancer in a mammal, which method comprises administering to a mammal having cancer an anticancer effective amount of a compound of claim 63, whereupon the cancer in the mammal is treated, wherein the cancer expresses heat shock protein 90 (Hsp90).

79. (Amended) A method of treating cancer in a mammal, which method comprises administering to a mammal having cancer an anticancer effective amount of a compound of claim 65, whereupon the cancer in the mammal is treated, wherein the cancer expresses Hsp90.

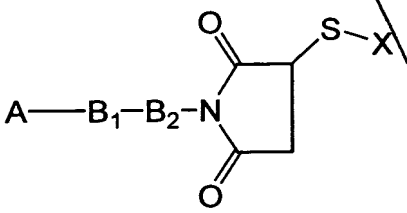
80. (Amended) A method of treating cancer in a mammal, which method comprises administering to a mammal having cancer an anticancer effective amount of a compound of claim 66, whereupon the cancer in the mammal is treated, wherein the cancer expresses Hsp90.

81. (Amended) A method of rendering soluble in water a water-insoluble drug, which method comprises:

(i) providing a water-insoluble drug comprising a side-chain that can react with a bifunctional linking molecule;

(ii) contacting said water-insoluble drug with said bifunctional linking molecule to obtain a first derivative comprising a maleimide side-chain; and

(iii) contacting said first derivative with a thio containing polar moiety (X-SH) to obtain a water-soluble compound of the formula



wherein:

A is a water-insoluble drug selected from the group consisting of a macrolide and an ansamacrolide;

B_1 and B_2 together are a spacer moiety,

wherein B_1 is selected from the group consisting of methylenyl, an amido, -N=, an amino, and a thiol maleimido, and

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Ho et al.

Application No. 09/743,873

Filed: April 18, 2001

Group Art Unit: 1624

Examiner: B. Kifle

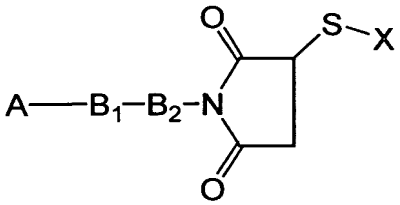
For: WATER-SOLUBLE DRUGS AND RELATED COMPOSITIONS AND METHODS OF PREPARING SAME

AMENDMENTS TO CLAIMS
MADE IN RESPONSE TO OFFICE ACTION DATED SEPTEMBER 6, 2002

(Deletions are indicated by bracketed text, while insertions are indicated by underlined text)

Please amend the following claims:

63. (Amended) A water-soluble compound of the formula



wherein:

A is a water-insoluble drug selected from the group consisting of a macrolide and an ansamacrolide;

B_1 and B_2 together are a spacer moiety,

wherein B_1 is selected from the group consisting of a methylenyl, an amido, -N=, an amino, and a thiol maleimido, and

B_2 is selected from the group consisting of a C_1-C_{19} alkylamido, a C_1-C_{19} alkyl, a C_2-C_{19} alkenyl, a C_2-C_{19} alkynyl, a C_1-C_{19} hydroxyalkyl, a C_1-C_{19} alkyl carbamoyl, a C_1-C_{19} alkylcarbonyl, and an aralkyl, any of which can be further substituted with one or more substitutents, which can be the same or different, selected from the group consisting of a nitro, a halo, an azido, a hydroxy, an amido, and an amino group; and

X is a polar moiety selected from the group consisting of an amino acid, a peptide, a polypeptide, and a protein;

or a pharmaceutically acceptable salt of said compound.

64. (Canceled)

65. (Amended) The compound of claim [64] 63, wherein

B_2 is selected from the group consisting of a C_1-C_7 alkylamido, a C_1-C_7 alkyl, a C_2-C_7 alkenyl, a C_2-C_7 alkynyl, a C_1-C_7 hydroxyalkyl, a C_1-C_7 alkyl carbamoyl, a C_1-C_7 alkylcarbonyl, and an aralkyl, any of which can be further substituted with one or more substituents, which can be the same or different, selected from the group consisting of a nitro, a halo, an azido, a hydroxy, an amido and an amino group.

67. (Canceled)

68. (Amended) The compound of claim [67] 63, wherein said polar moiety is L-cysteine.

71. (Canceled)

74. (Canceled)

77. (Amended) A method of treating cancer in a mammal, which method comprises administering to a mammal having cancer an anticancer effective amount of a compound of claim 63, whereupon the cancer in the mammal is treated, wherein the cancer expresses heat shock protein 90 (Hsp90).

78. (Canceled)

79. (Amended) A method of treating cancer in a mammal, which method comprises administering to a mammal having cancer an anticancer effective amount of a compound of claim 65, whereupon the cancer in the mammal is treated, wherein the cancer expresses Hsp90.

80. (Amended) A method of treating cancer in a mammal, which method comprises administering to a mammal having cancer an anticancer effective amount of a

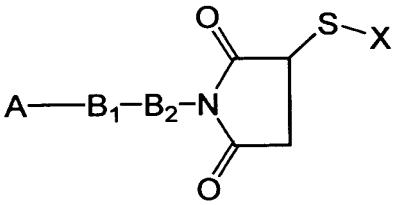
compound of claim 66, whereupon the cancer in the mammal is treated, wherein the cancer expresses Hsp90.

81. (Amended) A method of rendering soluble in water a water-insoluble drug, which method comprises:

(i) providing a water-insoluble drug comprising a side-chain that can react with a bifunctional linking molecule;

(ii) contacting said water-insoluble drug with said bifunctional linking molecule to obtain a first derivative comprising a maleimide side-chain; and

(iii) contacting said first derivative with a thio containing polar moiety (X-SH) to obtain a water-soluble compound of the formula



wherein:

A is a water-insoluble drug selected from the group consisting of a macrolide and an ansamacrolide;

B_1 and B_2 together are a spacer moiety,

wherein B_1 is selected from the group consisting of methylenyl, an amido, -N=, an amino, and a thiol maleimido, and

B_2 is selected from the group consisting of a C_1-C_{19} alkylamido, a C_1-C_{19} alkyl, a C_2-C_{19} alkenyl, a C_2-C_{19} alkynyl, a C_1-C_{19} hydroxyalkyl, a C_1-C_{19} alkyl carbamoyl, a C_1-C_{19} alkylcarbonyl, and an aralkyl, any of which can be further substituted with one or more substituents, which can be the same or different, selected from the group consisting of a nitro, a halo, an azido, a hydroxy, an amido and an amino group; and

X is a polar moiety selected from the group consisting of an amino acid, a polypeptide and a protein;

or a pharmaceutically acceptable salt of said compound.

82. (Canceled)

83. (Amended) The method of claim [82] 81, wherein

B_2 is selected from the group consisting of a C_1-C_7 alkylamido, a C_1-C_7 alkyl, a C_2-C_7 alkenyl, a C_2-C_7 alkynyl, a C_1-C_7 hydroxyalkyl, a C_1-C_7 alkyl carbamoyl, a C_1-C_7 alkylcarbonyl, and an aralkyl, any of which can be further substituted with one or more

substituents, which can be the same or different, selected from the group consisting of a nitro, a halo, an azido, a hydroxy, an amido, and an amino group.

88. (Canceled)

89. (Canceled)

92. (Canceled)

93. (Canceled)

94. (Canceled)

95. (Canceled)

96. (Canceled)

97. (Canceled)

98. (Canceled)

99. (Canceled)

100. (Canceled)

101. (Canceled)

102. (Canceled)

103. (Canceled)

104. (Canceled)

105. (Canceled)

106. (Canceled)